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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/578,290	01/11/2007	Robert Edward Coleman	33540-US-PCT	2763

1095 7590 06/17/2009

NOVARTIS
CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
SZNAIDMAN, MARCOS L	

ART UNIT	PAPER NUMBER
1612	

MAIL DATE	DELIVERY MODE
06/17/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/578,290	COLEMAN ET AL.	
	Examiner	Art Unit	
	MARCOS SZNAIDMAN	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7,11-13,26 and 28-31* is/are pending in the application.

4a) Of the above claim(s) *12 and 13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7,11,26 and 28-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1 page / 04/27/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This is office action is in response to applicant's request for continued examination filed on April 27, 2009.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114.

Status of Claims

Addition of claims 29-31 is acknowledged.

Claims 7, 11-13, 26 and 28-31 are currently pending and are the subject of this office action.

Claims 12 and 13 were withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on January 25, 2008

Claims 7, 11, 26 and 28-31 are presently under examination.

The following species is currently under examination: paclitaxel as the chemotherapeutic agent.

Priority

The present application is a 371 of PCT/EP04/13728 filed on 12/02/2004, and claims priority to foreign application: UNITED KINGDOM No. 0328040 filed on 08/04/2003.

Rejections and/or Objections and Response to Arguments

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated (Maintained Rejections and/or Objections) or newly applied (New Rejections and/or Objections, Necessitated by Amendment or New Rejections and/or Objections not Necessitated by Amendment). They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103 (Maintained Rejection)

Claims 7, 11, 26 and 28 and new claims 29-31 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Jagdev et. al. (British Journal of Cancer (2001) 84:1126-1134).

The reasons for this rejection have been provided in the previous office action dated January 6, 2009 the text of which is incorporated by reference herein.

Applicant's arguments have been fully considered but are not persuasive.

Applicant argues that: the concentration of Zoledronic acid (ZOL) of 10 micromolar and up and an incubation period of 72 hours for ZOL and PAC (paclitaxel) taught by Jagdev are not clinically relevant and that the instant Application uses clinically relevant concentrations and exposure times of ZOL and PAC.

Examiner's response: First, Jagdev also teaches that cells were also incubated with increasing concentrations of PAC alone and in combination with increasing concentrations of ZOL for a total of 72 hours to enable construction of isobolograms (see page 1127, under Measurement of cell number). On page 1130 Jagdev further discusses the synergistic effects of this combination (see last paragraph on left column) and in Figures 5I and 5II on page 1131 they show the dose response curves and isobologram plots for the interaction between PAC and ZOL on MCF7 cell number and apoptosis. In those graphs they show different combinations of PAC and ZOL: the concentrations of ZOL covers from 0 to 100 micromolar and they specifically teach ZOL concentrations below 10 micromolar like: 0.010 micromolar, 0.10 micromolar and 1 micromolar which can now be translated into an effective amount as recited by the instant claims.

Second: even if the above concentrations had not been disclosed, the skilled in the art would have been able to adjust any *in vitro* regimen to an *in vivo* regimen according to efficacy, toxicity and the and pharmacokinetic properties of a particular drug, and thus obtain an efficacious dose regimen. The experiments run by Jagdev are *in vitro* experiments, simply to show the synergistic properties of a combination of PAC

and ZOL, and as such the skilled in the art will translate and modify these amounts and periods of treatment according to the factors discussed above.

Applicant further argues that: in a second experiment a synergistic effect (4.1% on the apoptosis of breast cancer cells) was observed compared to either drug alone when the cells were exposed to 1 micromolar ZOL for 1 hour period (72 shorter than Jadgev) after the cells were exposed to PAC (2 nM, 4 hours, 18 times shorter than Jadgev).

Examiner's response: the synergistic effect presented by Applicant of 4.1% translates in 3.3 fold increase compared to PAC alone (see Experiment 2, on page 16 of the specification) or 16 fold increase compared to ZOL alone. Jagdev teaches a 5-fold increase in apoptosis compared with ZOL alone and a 4-fold increase compared with PAC alone (see page 1130, left column), which is very close to the synergism claimed by Applicant. Regarding the difference in time, the skilled in the art would definitively adjust the timing of the dose according to a patient requirement. Since Jagdev already teaches that a combination of ZOL and PAC is synergistic for the treatment of breast cancer, it will be expected that any form of dosage of these two active ingredients, whether they are administered simultaneously (like Jadgev teaches) or sequentially (like in the instant Application) will still be synergistic. So there is nothing in the claims and/or specification that show any unexpected result based on what is disclosed and taught by Jadgev.

Applicant finally argues that the Examiner's comment that Applicants have failed to show the synergistic effect over a wide range of concentrations has no bearing on the obviousness or patentability of the claimed methods. As shown above, Applicants tested the sequential administration of PAC and ZOL at clinically relevant concentrations and exposure times whereas Jagdev et al. did not.

Examiner's response: First: as discussed above, Jagdev does teach clinically relevant concentrations of ZOL.

Second: as mentioned in the previous Office Action, Applicant only provides data for a couple of concentrations of the combined drugs: 25 micromolar of ZOL acid and 2 nanomolar of PAC (see experiment 1 on page 15) and 1 micromolar ZOL acid and 2 nanomolar of PAC (see experiment 2 on page 15), as opposed to the wide range of concentrations taught by Jagdev ((0 to 100 micromolar of ZOL and 0 to 10 micromolar of PAC, see Figures 5I and 5II on page 1131) . The data presented by Applicant is not commensurate with the scope of the claims in which essentially there is no limitation on the concentrations of any of the active agents.

Third: even if Applicant were able to demonstrate synergism over a much wider set of concentrations, these results would not be unexpected based on the teachings of Jadgev.

Conclusion

No claims are allowed.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARCOS SZNAIDMAN whose telephone number is (571)270-3498. The examiner can normally be reached on Monday through Thursday 8 AM to 6 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick F. Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/MARCOS SZNAIDMAN/
Examiner, Art Unit 1612
June 11, 2009.

/Brandon J Fetterolf/

Primary Examiner, Art Unit 1642